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EXAMINER

OH, SIMON J

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1618

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/625,244

Filing Date: July 23, 2003

Appellant(s): PERRICONE, NICHOLAS V.

Stephen P. McNamara
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 07 November 2006 appealing from the Office action

mailed 28 June 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,261,598 Runge et al. 07-2001

DE 41 10087 A1 Woerwag et al. 10-1992

"Arthritis and Rheumatic Diseases" NIH Publication No. 02-4999

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 10-18 and 21-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Runge *et al.* in view of Woerwag *et al.*

The Runge *et al.* patent teaches carotenoid formulations for use in foods, cosmetics, and pharmaceuticals (See Abstract). The formulations may contain 0.01% to 40% by weight of various ingredients and combinations thereof, including vitamins such as tocotrienol, and allithiamines, such as benfotiamine (See Column 2, Lines 41-61; and Column 3, Lines 3-4). The formulations may comprise other ancillary substances and additives, such as physiologically acceptable oils (See Column 3, Lines 8-18). Minor amounts of stabilizers may also be added, such as α -tocopherol and ascorbic acid (See Column 3, Lines 31-41). Emulsifiers or solubilizers such as lecithin may also be added from 0% to 200% by weight of the carotenoids included in the formulation. Cosmetic formulations according to the disclosed invention include topical preparations, such as creams, lotions, emulsions, and suspensions (See Column 4, Lines 33-38).

The Runge *et al.* patent does not explicitly teach methods of treating skin damage.

The Woerwag *et al.* document discloses benfotiamine formulations comprising a carrier and applied topically to the skin for the treatment of various disorders, such as rheumatic disorders, and shingles.

It would be obvious to one of ordinary skill in the art to combine the prior art references in order to obtain the instantly claimed invention. As both references disclose topical compositions containing benfotiamine and auxiliary ingredients, it the position of the examiner that one of ordinary skill would find it obvious to combine the prior art references, and that the composition arising from the collective disclosure of the prior art would contain the benefits

found in each reference. The composition disclosed in the Runge *et al.* patent reads upon the breadth of the instant claim language, and furthermore discloses the composition as being useful as a cosmetic. It is the position of the examiner that one of ordinary skill in the art would, in light of such a disclosure, attribute the cosmetic composition as being useful for treating skin aging and/or improving the appearance of skin, with a reasonable expectation of success. The Woerwag *et al.* document discloses that the benfotiamine compositions are useful for treating rheumatic disorders and shingles, conditions that are known in the art to cause damage to skin. Therefore, one of ordinary skill in the art would be able to use the compositions of the prior art to treat skin damage with a reasonable expectation of success.

Thus, the instantly claimed invention is *prima facie* obvious.

(10) Response to Argument

The applicant's primary argument against the Woerwag *et al.* reference is that it discloses that the composition is disclosed to pass through the skin and treat an area underneath the skin rather than acting directly on the skin as recited by the instant claims. However, the examiner does not agree with the applicant's argument that if the benfotiamine passes through the skin as disclosed in Woerwag *et al.*, then that therefore must mean that it does so without affecting it in any manner. The applicant attempts to establish a scenario where either a topical benfotiamine composition acts directly upon the skin and all of the active agent is expended only at the skin, or that a topical benfotiamine composition is applied and the active agent passes through the skin without affecting it in any manner and acts only below the surface of the skin. In such a scenario, only one of these outcomes is possible, without considering that a combination of these

possibilities is even possible. Furthermore, the applicant has not provided any sort of evidence that either premise is valid to the complete exclusion of the other.

The prior art has generally shown that benfotiamine is useful in treating conditions exhibited by symptoms of skin inflammation. Therefore, in the view of the examiner, the prior art broadly discloses that such prior art compositions and methods are useful for improving the appearance of the skin, which are broadly within the same field of endeavor as the instant claims. The applicant bases the patentability of the instant claims upon the action of the reduction of glycated proteins, which appears to be a new or previously unknown property of benfotiamine as a topical active agent, where the prior art has used the active agent in the same capacity in a topical formulation. However, such a previously unknown property does not render the instant claims patentable. See MPEP § 2112.

On the topic of an overlap in patient populations between those that would be likely treated by the methods of the prior art and the instantly claimed methods, the applicant is correct when citing the NIH publication that rheumatic disorders affect people of all ages. However, the publication also cites that it is the leading cause of disability among adults age 65 and over (See page 6 of NIH Publication No. 02-4999). Because of its prevalence among the elderly, the examiner finds this argument by the applicant unpersuasive and will therefore maintain the statement regarding an overlap in patient populations.

As such, the prior art rejections of record are maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

Art Unit: 1618

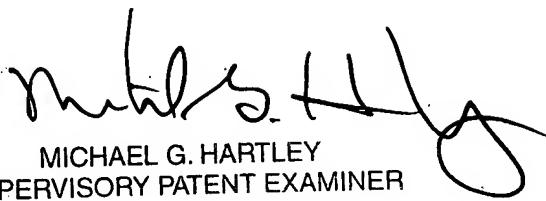
For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

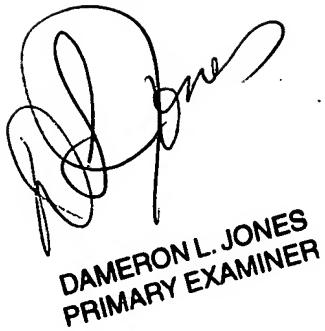
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*Questions
& Answers*

about . . .

Arthritis and Rheumatic Diseases

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

National Institutes of Health

Public Health Service • U.S. Department of Health and Human Services

For Your Information

This publication contains information about medications used to treat the health condition discussed in this booklet. When this booklet was printed, we included the most up-to-date (accurate) information available. Occasionally, new information on medication is released.

For updates and for any questions about any medications you are taking, please contact the U.S. Food and Drug Administration at 1-888-INFO-FDA (1-888-463-6332, a toll-free call) or visit their Web site at www.fda.gov.

This booklet is not copyrighted. Readers are encouraged to duplicate and distribute as many copies as needed.

Additional copies of this booklet are available from

National Institute of Arthritis and Musculoskeletal
and Skin Diseases
NIAMS/National Institutes of Health
1 AMS Circle
Bethesda, MD 20892-3675

You can also find this booklet on the NIAMS Web site
[at www.niams.nih.gov/hi/topics/arthritis/artrheu.htm](http://www.niams.nih.gov/hi/topics/arthritis/artrheu.htm).

Arthritis and Rheumatic Diseases

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Arthritis and Rheumatic Diseases

This booklet answers basic questions about arthritis and rheumatic diseases. The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) has other fact sheets and booklets that provide more information about specific forms of arthritis and rheumatic diseases. NIAMS also has information about exercise and arthritis, pain and arthritis, and diet and arthritis.

If you have further questions after reading this information, you may wish to discuss them with your doctor.

What Are Rheumatic Diseases and What Is Arthritis?

Rheumatic diseases are characterized by inflammation (signs are redness and/or heat, swelling, and pain) and loss of function of one or more connecting or supporting structures of the body. They especially affect joints, tendons, ligaments, bones, and muscles. Common symptoms are pain, swelling, and stiffness. Some rheumatic diseases can also involve internal organs. There are more than 100 rheumatic diseases.

Many people use the word "arthritis" to refer to all rheumatic diseases. However, the word literally means joint inflammation. The many different kinds of arthritis comprise just a portion of the rheumatic diseases. Some rheumatic diseases are described as connective tissue diseases because

they affect the supporting framework of the body and its internal organs. Others are known as autoimmune diseases because they occur when the immune system, which normally protects the body from infection and disease, harms the body's own healthy tissues. Throughout this booklet the terms "arthritis" and "rheumatic diseases" are sometimes used interchangeably.

Examples of Rheumatic Diseases

Osteoarthritis—This is the most common type of arthritis, affecting an estimated 21 million adults in the United States. Osteoarthritis primarily affects cartilage, which is the tissue that cushions the ends of bones within the joint. In osteoarthritis, the cartilage begins to fray and may entirely wear away. Osteoarthritis can cause joint pain and stiffness. Disability results most often when the disease affects the spine and the weight-bearing joints (the knees and hips).

Rheumatoid arthritis—This inflammatory disease of the synovium, or lining of the joint, results in pain, stiffness, swelling, joint damage, and loss of function of the joints. Inflammation most often affects joints of the hands and feet and tends to be symmetrical (occurring equally on both sides of the body). This symmetry helps distinguish rheumatoid arthritis from other forms of the disease. About 1 percent of the U.S. population (about 2.1 million people) has rheumatoid arthritis.

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Juvenile rheumatoid arthritis—This is the most common form of arthritis in childhood, causing pain, stiffness, swelling, and loss of function of the joints. The arthritis may be associated with rashes or fevers, and may affect various parts of the body.

Fibromyalgia—Fibromyalgia is a chronic disorder that causes pain throughout the tissues that support and move the bones and joints. Pain, stiffness, and localized tender points occur in the muscles and tendons, particularly those of the neck, spine, shoulders, and hips. Patients may also experience fatigue and sleep disturbances.

Systemic lupus erythematosus—Systemic lupus erythematosus (also known as lupus or SLE) is an autoimmune disease in which the immune system harms the body's own healthy cells and tissues. This can result in inflammation of and damage to the joints, skin, kidneys, heart, lungs, blood vessels, and brain.

Scleroderma—Also known as systemic sclerosis, scleroderma means literally “hard skin.” The disease affects the skin, blood vessels, and joints. It may also affect internal organs, such as the lungs and kidneys. In scleroderma, there is an abnormal and excessive production of collagen (a fiber-like protein) in the skin or internal organs.

Spondyloarthropathies—This group of rheumatic diseases principally affects the spine. One common form—ankylosing spondylitis—not only affects the spine, but may also affect the hips, shoulders, and knees as the tendons and

ligaments around the bones and joints become inflamed, resulting in pain and stiffness. Ankylosing spondylitis tends to affect people in late adolescence or early adulthood.

Reactive arthritis, sometimes called Reiter's syndrome, is another spondyloarthropathy. It develops after an infection involving the lower urinary tract, bowel, or other organ and is commonly associated with eye problems, skin rashes, and mouth sores.

Gout—This type of arthritis results from deposits of needle-like crystals of uric acid in the joints. The crystals cause inflammation, swelling, and pain in the affected joint, which is often the big toe.

Infectious arthritis—This is a general term used to describe forms of arthritis that are caused by infectious agents, such as bacteria or viruses. Parvovirus arthritis and gonococcal arthritis are examples of infectious arthritis. Arthritis symptoms may also occur in Lyme disease, which is caused by a bacterial infection following the bite of certain ticks. In those cases of arthritis caused by bacteria, early diagnosis and treatment with antibiotics are crucial to get rid of the infection and minimize damage to the joints.

Polymyalgia rheumatica—Because this disease involves tendons, muscles, ligaments, and tissues around the joint, symptoms often include pain, aching, and morning stiffness in the shoulders, hips, neck, and lower back. It is sometimes the first sign of giant cell arteritis, a disease of the arteries characterized by inflammation, weakness, weight loss, and fever.

Arthritis and Rheumatic Diseases

Polymyositis—This is a rheumatic disease that causes inflammation and weakness in the muscles. The disease may affect the whole body and cause disability.

Psoriatic arthritis—This form of arthritis occurs in some patients with psoriasis, a scaling skin disorder. Psoriatic arthritis often affects the joints at the ends of the fingers and toes and is accompanied by changes in the fingernails and toenails. Back pain may occur if the spine is involved.

Bursitis—This condition involves inflammation of the bursae, small, fluid-filled sacs that help reduce friction between bones and other moving structures in the joints. The inflammation may result from arthritis in the joint or injury or infection of the bursae. Bursitis produces pain and tenderness and may limit the movement of nearby joints.

Tendinitis (Tendonitis)—This condition refers to inflammation of tendons (tough cords of tissue that connect muscle to bone) caused by overuse, injury, or a rheumatic condition. Tendinitis produces pain and tenderness and may restrict movement of nearby joints.

What Causes Rheumatic Disease?

Scientists are studying risk factors that increase the likelihood of developing a rheumatic disease. Some of these factors have been identified. For example, in osteoarthritis, inherited cartilage weakness or excessive stress on the joint from repeated injury may play a role. In lupus, rheumatoid

arthritis, and scleroderma, the combination of genetic factors that determine susceptibility and environmental triggers are believed to be important. Family history also plays a role in some diseases such as gout and ankylosing spondylitis.

Gender is another factor in some rheumatic diseases. Lupus, rheumatoid arthritis, scleroderma, and fibromyalgia are more common among women. (See next section for details.) This indicates that hormones or other male-female differences may play a role in the development of these conditions.

Who Is Affected by Arthritis and Rheumatic Conditions?

An estimated 43 million people in the United States have arthritis or other rheumatic conditions. By the year 2020, this number is expected to reach 60 million. Rheumatic diseases are the leading cause of disability among adults age 65 and older.

Rheumatic diseases affect people of all races and ages. Some rheumatic conditions are more common among certain populations. For example:

- Rheumatoid arthritis occurs two to three times more often in women than in men.
- Scleroderma is more common in women than in men.

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- Nine out of 10 people who have lupus are women.
- Nine out of 10 people who have fibromyalgia are women.
- Gout is more common in men than in women.
- Lupus is three times more common in African American women than in Caucasian women.
- Ankylosing spondylitis is more common in men than in women.

What Are the Symptoms of Arthritis?

Different types of arthritis have different symptoms. In general, people who have arthritis feel pain and stiffness in the joints. Some of the more common symptoms are listed in the box on page 8. Early diagnosis and treatment help decrease further joint damage and help control symptoms of arthritis and many other rheumatic diseases.

How Are Rheumatic Diseases Diagnosed?

Diagnosing rheumatic diseases can be difficult because some symptoms and signs are common to many different diseases. A general practitioner or family doctor may be able to evaluate a patient or refer him or her to a rheumatologist (a doctor who specializes in treating arthritis and other rheumatic diseases).

Common Symptoms of Arthritis

- Swelling in one or more joints
- Stiffness around the joints that lasts for at least 1 hour in the early morning
- Constant or recurring pain or tenderness in a joint
- Difficulty using or moving a joint normally
- Warmth and redness in a joint

The doctor will review the patient's medical history, conduct a physical examination, and obtain laboratory tests and x rays or other imaging tests. The doctor may need to see the patient more than once to make an accurate diagnosis.

Medical History

It is vital for people with joint pain to give the doctor a complete medical history. Answers to the following questions will help the doctor make an accurate diagnosis:

- Is the pain in one or more joints?
- When does the pain occur?
- How long does the pain last?
- When did you first notice the pain?

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- What were you doing when you first noticed the pain?
- Does activity make the pain better or worse?
- Have you had any illnesses or accidents that may account for the pain?
- Is there a family history of arthritis or other rheumatic disease?
- What medicine(s) are you taking?

Because rheumatic diseases are so diverse and sometimes involve several parts of the body, the doctor may ask many other questions.

It may be helpful for people to keep a daily journal that describes the pain. Patients should write down what the affected joint looks like, how it feels, how long the pain lasts, and what they were doing when the pain started.

Physical Examination and Laboratory Tests

The doctor will examine the patient's joints for redness, warmth, damage, ease of movement, and tenderness. Because some forms of arthritis, such as lupus, may affect other organs, a complete physical examination that includes the heart, lungs, abdomen, nervous system, eyes, ears, and throat may be necessary. The doctor may order some laboratory tests to help confirm a diagnosis. Samples of blood,

urine, or synovial fluid (lubricating fluid found in the joint) may be needed for the tests.

Common laboratory tests and procedures include the following:

Antinuclear antibody (ANA)—This test checks blood levels of antibodies that are often present in people who have connective tissue diseases or other autoimmune disorders, such as lupus. Since the antibodies react with material in the cell's nucleus (control center), they are referred to as anti-nuclear antibodies. There are also tests for individual types of ANAs that may be more specific to people with certain autoimmune disorders. ANAs are also sometimes found in people who do not have an autoimmune disorder. Therefore, having ANAs in the blood does not necessarily mean that a person has a disease.

C-reactive protein test—This is a nonspecific test used to detect generalized inflammation. Levels of the protein are often increased in patients with active disease such as rheumatoid arthritis, and may decline when corticosteroids or nonsteroidal anti-inflammatory drugs (NSAIDs) are used to reduce inflammation.

Complement—This test measures the level of complement, a group of proteins in the blood. Complement helps destroy foreign substances, such as germs, that enter the body. A low blood level of complement is common in people who have active lupus.

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Complete blood count (CBC)—This test determines the number of white blood cells, red blood cells, and platelets present in a sample of blood. Some rheumatic conditions or drugs used to treat arthritis are associated with a low white blood count (leukopenia), low red blood count (anemia), or low platelet count (thrombocytopenia). When doctors prescribe medications that affect the CBC, they periodically test the patient's blood.

Creatinine—This blood test is commonly ordered in patients who have a rheumatic disease, such as lupus, to monitor for underlying kidney disease. Creatinine is a breakdown product of creatine, which is an important component of muscle. It is excreted from the body entirely by the kidneys, and the level remains constant and normal when kidney function is normal.

Erythrocyte sedimentation rate (“sed rate”)—This blood test is used to detect inflammation in the body. Higher sed rates indicate the presence of inflammation and are typical of many forms of arthritis, such as rheumatoid arthritis and ankylosing spondylitis, and many of the connective tissue diseases.

Hematocrit (PCV, packed cell volume)—This test and the test for hemoglobin (a substance in the red blood cells that carries oxygen throughout the body) measure the number of red blood cells present in a sample of blood. A decrease in the number of red blood cells (anemia) is common in people



who have inflammatory arthritis or another rheumatic disease.

Rheumatoid factor—This test detects the presence of rheumatoid factor, an antibody found in the blood of most (but not all) people who have rheumatoid arthritis.

Rheumatoid factor may be found in many diseases besides rheumatoid arthritis, and sometimes in people without health problems.

Synovial fluid examination—Synovial fluid may be examined for white blood cells (found in patients with rheumatoid arthritis and infections), bacteria or viruses (found in patients with infectious arthritis), or crystals in the joint (found in patients with gout or other types of crystal-induced arthritis). To obtain a specimen, the doctor injects a local anesthetic, then inserts a needle into the joint to withdraw the synovial fluid into a syringe. The procedure is called arthrocentesis or joint aspiration.

Urinalysis—In this test, a urine sample is studied for protein, red blood cells, white blood cells, and bacteria. These abnormalities may indicate kidney disease, which may be seen in several rheumatic diseases, including lupus. Some medications used to treat arthritis can also cause abnormal findings on urinalysis.

White blood cell count (WBC)—This test determines the number of white blood cells present in a sample of blood. The number may increase as a result of infection or decrease in response to certain medications or in certain diseases,

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such as lupus. Low numbers of white blood cells increase a person's risk of infections.

X Rays and Other Imaging Procedures

To see what the joint looks like inside, the doctor may order x rays or other imaging procedures. X rays provide an image of the bones, but they do not show cartilage, muscles, and ligaments. Other noninvasive imaging methods such as computed tomography (CT or CAT scan), magnetic resonance imaging (MRI), and arthrography show the whole joint. The doctor may look for damage to a joint by using an arthroscope, a small, flexible tube which is inserted through a small incision at the joint and which transmits the image of the inside of a joint to a video screen.

What Are the Treatments?

Treatments for rheumatic diseases include rest and relaxation, exercise, proper diet, medication, and instruction about the proper use of joints and ways to conserve energy. Other treatments include the use of pain relief methods and assistive devices, such as splints or braces. In severe cases, surgery may be necessary. The doctor and the patient work together to develop a treatment plan that helps the patient maintain or improve his or her lifestyle. Treatment plans usually combine several types of treatment and vary depending on the rheumatic condition and the patient.

Rest, Exercise, and Diet

People who have a rheumatic disease should develop a comfortable balance between rest and activity. One sign of many rheumatic conditions is fatigue. Patients must pay attention to signals from their bodies. For example, when experiencing pain or fatigue, it is important to take a break and rest. Too much rest, however, may cause muscles and joints to become stiff.

People with a rheumatic disease such as arthritis can participate in a variety of sports and exercise programs. Physical exercise can reduce joint pain and stiffness and increase flexibility, muscle strength, and endurance. It also helps with weight reduction and contributes to an improved sense of well-being. Before starting any exercise program, people with arthritis should talk with their doctor. Exercises that doctors often recommend include:

- Range-of-motion exercises (e.g., stretching, dance) to help maintain normal joint movement, maintain or increase flexibility, and relieve stiffness.
- Strengthening exercises (e.g., weight lifting) to maintain or increase muscle strength. Strong muscles help support and protect joints affected by arthritis.
- Aerobic or endurance exercises (e.g., walking, bicycle riding) to improve cardiovascular fitness, help control weight, and improve overall well-being. Studies

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show that aerobic exercise can also reduce inflammation in some joints.

Another important part of a treatment program is a well-balanced diet. Along with exercise, a well-balanced diet helps people manage their body weight and stay healthy. Weight control is important to people who have arthritis because extra weight puts extra pressure on some joints and can aggravate many types of arthritis. Diet is especially important for people who have gout. People with gout should avoid alcohol and foods that are high in purines, such as organ meats (liver, kidney), sardines, anchovies, and gravy.

Medications

A variety of medications are used to treat rheumatic diseases. The type of medication depends on the rheumatic disease and on the individual patient. The medications used to treat most rheumatic diseases do not provide a cure, but rather limit the symptoms of the disease. Infectious arthritis and gout are exceptions if medications are used properly. Another example is Lyme disease, caused by the bite of certain ticks, where symptoms of arthritis may be prevented or may disappear if the infection is caught early and treated with antibiotics.

Medications commonly used to treat rheumatic diseases provide relief from pain and inflammation. In some cases, the

medication may slow the course of the disease and prevent further damage to joints or other parts of the body.

The doctor may delay using medications until a definite diagnosis is made because medications can hide important symptoms (such as fever and swelling) and thereby interfere with diagnosis. Patients taking any medication, either prescription or over-the-counter, should always follow the doctor's instructions. The doctor should be notified immediately if the medicine is making the symptoms worse or causing other problems, such as an upset stomach, nausea, or headache. The doctor may be able to change the dosage or medicine to reduce these side effects.

Analgesics (pain relievers) such as acetaminophen (Tylenol)* and nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen are used to reduce the pain caused by many rheumatic conditions. NSAIDs have the added benefit of decreasing the inflammation associated with arthritis. A common side effect of NSAIDs is stomach irritation, which can often be reduced by changing the dosage or medication. New NSAIDs, such as celecoxib (Celebrex), were introduced to reduce gastrointestinal side effects and offer additional options for treatment. However, even new medications are occasionally associated with reactions ranging from mild to severe, and their long-term effects are still being studied. The dosage will vary depend-

* Brand names included in this booklet are provided as examples only, and their inclusion does not mean that these products are endorsed by the National Institutes of Health or any other Government agency. Also, if a particular brand name is not mentioned, this does not mean or imply that the product is unsatisfactory.

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ing on the particular illness and the overall health of the patient. The doctor and patient must work together to determine which analgesic to use and the appropriate amount. If analgesics do not ease the pain, the doctor may use other medications.

Depending on the type of arthritis, a person may be asked to take a disease-modifying antirheumatic drug (DMARD). This category includes several unrelated medications that are intended to slow or prevent damage to the joint and thereby prevent disability and discomfort. DMARDs include methotrexate, sulfasalazine, and leflunomide (Arava).

Biological response modifiers are new drugs used for the treatment of rheumatoid arthritis. They can help reduce inflammation and structural damage of the joints by blocking the reaction of a substance called tumor necrosis factor, a protein involved in immune system response. These drugs include etanercept (Enbrel), infliximab (Remicade), and anakinra (Kineret).

Corticosteroids, such as prednisone, cortisone, solumedrol, and hydrocortisone, are used to treat many rheumatic conditions because they decrease inflammation and suppress the immune system. The dosage of these medications will vary depending on the diagnosis and the patient. Again, the patient and doctor must work together to determine the right amount of medication.

Corticosteroids can be given by mouth, in creams applied to the skin, or by injection. Short-term side effects of corticosteroids include swelling, increased appetite, weight gain, and emotional ups and downs. These side effects generally stop when the drug is stopped. It can be dangerous to stop taking corticosteroids suddenly, so it is very important that the doctor and patient work together when changing the corticosteroid dose. Side effects that may occur after long-term use of corticosteroids include stretch marks, excessive hair growth, osteoporosis, high blood pressure, damage to the arteries, high blood sugar, infections, and cataracts.

Hyaluronic acid products like Hyalgan and Synvisc mimic a naturally occurring body substance that lubricates the knee joint. They are usually injected directly into the joint to help provide temporary relief of pain and flexible joint movement.

Devices Used in Treatment

Transcutaneous electrical nerve stimulation (TENS) has been found effective in modifying pain perception. TENS blocks pain messages to the brain with a small device that directs mild electric pulses to nerve endings that lie beneath the painful area of the skin.

A blood-filtering device called the Prosorba Column is used in some health care facilities for filtering out harmful antibodies in people with severe rheumatoid arthritis.

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Heat and Cold Therapies

Heat and cold can both be used to reduce the pain and inflammation of arthritis. The patient and doctor can determine which one works best.

Heat therapy increases blood flow, tolerance for pain, and flexibility. Heat therapy can involve treatment with paraffin wax, microwaves, ultrasound, or moist heat. Physical therapists are needed for some of these therapies, such as microwave or ultrasound therapy, but patients can apply moist heat themselves. Some ways to apply moist heat include placing warm towels or hot packs on the inflamed joint or taking a warm bath or shower.

Cold therapy numbs the nerves around the joint (which reduces pain) and may relieve inflammation and muscle spasms. Cold therapy can involve cold packs, ice massage, soaking in cold water, or over-the-counter sprays and ointments that cool the skin and joints.

Capsaicin cream is a preparation put on the skin to relieve joint or muscle pain when only one or two joints are involved.

Hydrotherapy, Mobilization Therapy, and Relaxation Therapy

Hydrotherapy involves exercising or relaxing in warm water. The water takes some weight off painful joints, making it easier to exercise. It helps relax tense muscles and relieve pain.

Mobilization therapies include traction (gentle, steady pulling), massage, and manipulation. (Someone other than the patient moves stiff joints through their normal range of motion.) When done by a trained professional, these methods can help control pain, increase joint motion, and improve muscle and tendon flexibility.

Relaxation therapy helps reduce pain by teaching people various ways to release muscle tension throughout the body. In one method of relaxation therapy, known as progressive relaxation, the patient tightens a muscle group and then slowly releases the tension. Doctors and physical therapists can teach patients a variety of relaxation techniques.

Assistive Devices

The most common assistive devices for treating arthritis pain are splints and braces, which are used to support weakened joints or allow them to rest. Some of these devices prevent the joint from moving; others allow some movement. A splint or brace should be used only when recommended by a doctor or therapist, who will show the patient the correct way to put the device on, ensure that it fits properly, and explain when and for how long it should be worn. The incorrect use of a splint or brace can cause joint damage, stiffness, and pain.

A person with arthritis can use other kinds of devices to ease the pain. For example, the use of a cane when walking can reduce some of the weight placed on a knee or hip affected

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by arthritis. A shoe insert (orthotic) can ease the pain of walking caused by arthritis of the foot or knee. Other devices can help with activities such as opening jars, closing zippers, and holding pencils.

Surgery

Surgery may be required to repair damage to a joint after injury or to restore function or relieve pain in a joint damaged by arthritis. The doctor may recommend arthroscopic surgery, bone fusion (surgery in which bones in the joint are fused or joined together), or arthroplasty (also known as total joint replacement, in which the damaged joint is removed and replaced with an artificial one).

Nutritional Supplements

Nutritional supplements are often reported as helpful in treating rheumatic diseases. These include products such as S-adenosylmethionine (SAM-e) for osteoarthritis and fibromyalgia, dehydroepiandrosterone (DHEA) for lupus, and glucosamine and chondroitin sulfate for osteoarthritis. Reports on the safety and effectiveness of these products should be viewed with caution since very few claims have been carefully evaluated.

Myths About Treating Arthritis

At this time, the only type of arthritis that can be cured is that caused by infections. Although symptoms of other types

of arthritis can be effectively managed with rest, exercise, and medication, there are no cures. Some people claim to have been cured by treatment with herbs, oils, chemicals, special diets, radiation, or other products. However, there is no scientific evidence that such treatments cure arthritis. Moreover, some may lead to serious side effects. Patients should talk to their doctor before using any therapy that has not been prescribed or recommended by the health care team caring for the patient.

Work With Your Doctor To Limit Your Pain

The role you play in planning your treatment is very important. It is vital for you to have a good relationship with your doctor in order to work together. You should not be afraid to ask questions about your condition or treatment. You must understand the treatment plan and tell the doctor whether or not it is helping you. Research has shown that patients who are well informed and participate actively in their own care experience less pain and make fewer visits to the doctor.

What Can Be Done To Help?

Studies show that an estimated 18 percent of Americans who have arthritis or other rheumatic conditions believe that their condition limits their activities. People with arthritis may find that they can no longer participate in some of their

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favorite activities, which can affect their overall well-being. Even when arthritis impairs only one joint, a person may have to change many daily activities to protect that joint from further damage and reduce pain. When arthritis affects the entire body, as it does in people with rheumatoid arthritis or fibromyalgia, many daily activities have to be changed to deal with pain, fatigue, and other symptoms.

Changes in the home may help a person with chronic arthritis continue to live safely, productively, and with less pain. People with arthritis may become weak, lose their balance, or fall. In the bathroom, installing grab bars in the tub or shower and by the toilet, placing a secure seat in the tub, and raising the height of the toilet seat can help. Special kitchen utensils can accommodate hands affected by arthritis to make meal preparation easier. An occupational therapist can help people who have rheumatic conditions identify and make adjustments in their homes to create a safer, more comfortable, and more efficient environment.

Friends and family members can help a patient with a rheumatic condition by learning about that condition and understanding how it affects the patient's life. Friends and family can provide emotional and physical assistance. Their support, as well as support from other people who have the same disease, can make it easier to cope. The Arthritis Foundation has a wealth of information to help people with arthritis. (See the list of resources at the end of this booklet.)

What Research Is Being Done on Arthritis?

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a part of the National Institutes of Health (NIH), leads the Federal medical research effort in arthritis and rheumatic diseases. The NIAMS sponsors research and research training on the NIH campus in Bethesda, Maryland, and at universities and medical centers throughout the United States. Research activities include both basic (laboratory) and clinical (involving patients) research studies to better understand what causes these conditions and how best to treat and prevent them.

The NIAMS currently supports three types of research centers that study arthritis, rheumatic diseases, and other musculoskeletal conditions: Multidisciplinary Clinical Research Centers (MCRCs), Specialized Centers of Research (SCORs), and Core Centers. A list of these centers and their locations can be obtained from the Institute (listed at the end of this booklet).

The MCRCs are programs that focus on clinical research designed to assess and improve outcomes for patients affected by arthritis and other rheumatic diseases, musculoskeletal disorders (including bone and muscle diseases), and skin diseases. Each center studies one or more of the diseases within the NIAMS mission and provides resources for developing clinical projects using more than one approach.

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Each SCOR focuses on a single disease. Currently, rheumatoid arthritis, systemic lupus erythematosus, osteoarthritis, osteoporosis, and scleroderma are being studied. Combining laboratory and clinical studies under one roof speeds up research on the causes of these diseases and hastens transfer of advances from the laboratory to the bedside to improve patient care.

Core Centers promote interdisciplinary collaborative efforts among scientists doing high-quality research related to a common theme. By providing funding for facilities, pilot and feasibility studies, and program enrichment activities at the Core Center, the Institute reinforces investigations already underway in NIAMS program areas. Current centers include Rheumatic Diseases Research Core Centers, Skin Disease Research Core Centers, and Core Centers for Musculoskeletal Disorders.

Research registries provide a means for collecting clinical, demographic, and laboratory information from patients and, sometimes, their relatives. These registries facilitate studies that could ultimately lead to improved diagnosis, treatment, and prevention. NIAMS currently supports research registries for rheumatoid arthritis, antiphospholipid syndrome (an autoimmune disorder), ankylosing spondylitis, lupus and neonatal lupus, scleroderma, juvenile rheumatoid arthritis, and juvenile dermatomyositis.

Some current NIAMS research efforts in rheumatic diseases are outlined below.

Biomarkers

Recent scientific breakthroughs in basic research have provided new information about what happens to the body's cells and other structures as rheumatic diseases progress. Biomarkers (laboratory and imaging signposts that detect disease) help researchers determine the likelihood that a person will develop a specific disease and its possible severity and outcome. Biomarkers have the potential to lead to novel and more effective ways to predict and monitor disease activity and responses to treatment. The NIAMS supports research on biomarkers for rheumatic and skin diseases, including a new initiative on osteoarthritis. Additional studies on specific rheumatic diseases follow.

Rheumatoid Arthritis

Researchers are trying to identify the cause of rheumatoid arthritis in order to develop better and more specific treatments. They are examining the role that the endocrine (hormonal), nervous, and immune systems play, and the ways in which these systems interact with environmental and genetic factors in the development of rheumatoid arthritis. Some scientists are trying to determine whether an infectious agent triggers rheumatoid arthritis. Others are studying the role of certain enzymes (specialized proteins in the body that spark biochemical reactions) in breaking down

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cartilage. Researchers are also trying to identify the genetic factors that place some people at higher risk than others for developing rheumatoid arthritis.

Moreover, scientists are looking at new ways to treat rheumatoid arthritis. They are experimenting with new drugs and "biologic agents" that selectively block certain immune system activities associated with inflammation. Newly developed drugs include etanercept (Enbrel) and infliximab (Remicade). Followup studies show promise for their effectiveness in slowing disease progression. Studies for additional new drugs continue. Other investigators have shown that minocycline and doxycycline, two antibiotic medications in the tetracycline family, have a modest benefit for people with rheumatoid arthritis. Research continues in this area.

Novel studies using imaging technologies are underway as well. These techniques help identify targets for new drugs by allowing researchers to see changes in cells during the disease process.

Osteoarthritis

The NIAMS has embarked on several innovative approaches to understand the causes and identify effective treatment and prevention methods for osteoarthritis. Through a public/private partnership, researchers are identifying biomarkers for osteoarthritis to help develop and test new drugs.

Imaging studies designed to better identify joint disorders and assess their progression are taking place as well.

The National Center for Complementary and Alternative Medicine and the NIAMS at the National Institutes of Health are currently funding a study on the usefulness of the dietary supplements glucosamine and chondroitin sulfate for osteoarthritis. Previous studies suggest these substances may be effective for reducing pain in knee osteoarthritis. Researchers are also investigating whether they prevent the loss of cartilage.

Some genetic and behavioral studies are focusing on factors that may lead to osteoarthritis. Researchers recently found that daughters of women who have knee osteoarthritis have a significant increase in cartilage breakdown, thus making them more susceptible to disease. This finding has important implications for identifying people who are susceptible to osteoarthritis. Other studies of risk factors for osteoarthritis have identified excessive weight and lack of exercise as contributing factors to knee and hip disability.

Researchers are working to understand what role certain enzymes play in the breakdown of joint cartilage in osteoarthritis and are testing drugs that block the action of these enzymes.

Studies of injuries in young adults show that those who have had a previous joint injury are more likely to develop osteoarthritis. These studies underscore the need for

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increased education about joint injury prevention and use of proper sports equipment.

Systemic Lupus Erythematosus

Researchers are looking at how genetic, environmental, and hormonal factors influence the development of systemic lupus erythematosus. They are trying to find out why lupus is more common in certain populations, and they have made progress in identifying the genes that may be responsible for lupus. Researchers also continue to study the cellular and molecular basis of autoimmune disorders such as lupus. Promising areas of research on treatment include biologic agents; newer, more selective drugs that suppress the immune system; and bone transplants to correct immune abnormalities. Contrary to the widely held belief that estrogens can make the disease worse, clinical studies are revealing that it may be safe to use estrogens for hormone replacement therapy and birth control in women with lupus.

Scleroderma

Current studies on scleroderma are focusing on overproduction of collagen, blood vessel injury, and abnormal immune system activity. Researchers hope to discover how these three elements interact to cause and promote scleroderma. In one study, researchers found evidence of fetal cells within the blood and skin lesions of women who had been pregnant years before developing scleroderma. The study suggests that fetal cells may play a role in scleroderma by

fostering the maturation of immune cells that promote the overproduction of collagen. Scientists are continuing to study the implications of this finding.

Treatment studies are underway as well. One study in particular is looking at the effectiveness of oral collagen in treating scleroderma.

Fibromyalgia

Scientists are looking at the basic causes of chronic pain and the health status of young women affected by fibromyalgia. The effectiveness of behavior therapy, acupuncture, and some alternative medical approaches for dealing with pain and loss of sleep are being tested. Researchers are also studying whether certain genes contribute to this disease.

Spondyloarthropathies

Researchers are working to understand the genetic and environmental causes of spondyloarthropathies, which include ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease, and reactive arthritis (Reiter's syndrome), as well as related conditions of the eye. They are also looking at new imaging methods that will help with early and accurate diagnosis, guide treatment, and detect responses to treatment. Research on new treatments is also underway.

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The Health Partnership Program: A Local Diversity Outreach Initiative in the Rheumatic Diseases

In the winter of 2000, the NIAMS launched the Health Partnership Program (HPP), a local model of research and service that addresses disparities in preventing and treating rheumatic diseases in multicultural communities. The initiative focuses on four key areas: (1) public health education, (2) patient care, (3) access to clinical investigations, and (4) recruitment for research careers. The partnership includes community leaders and organizations representing the populations being served. They promote awareness of the program and its services and advise the Institute on community outreach activities.

One component of the HPP is the NIAMS Community Health Center located in Washington, DC. The health center provides a platform for conducting health disparities research by implementing the four key areas of the HPP. The center offers patients quality health care and health information in a community clinic setting. Patients are also given the option of participating in clinical studies. More information about the HPP is available at www.niams.nih.gov/hi/outreach/index.htm.

Where Can People Find More Information About Arthritis and Rheumatic Diseases?

- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)**

National Institutes of Health

1 AMS Circle

Bethesda, MD 20892-3675

Phone: 301-495-4484 or

877-22-NIAMS (226-4267) (free of charge)

TTY: 301-565-2966

Fax: 301-718-6366

E-mail: NIAMSIInfo@mail.nih.gov

www.niams.nih.gov

NIAMS provides information about various forms of arthritis and rheumatic diseases and bone, muscle, joint, and skin diseases. It distributes patient and professional education materials and refers people to other sources of information. Additional information and updates can be found on the NIAMS Web site. Listings of clinical trials recruiting patients who have or are at risk of developing a rheumatic disease can be found at www.ClinicalTrials.gov.

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- **American Academy of Orthopaedic Surgeons**
P.O. Box 2058
Des Plaines, IL 60017
Phone: 800-824-BONE (2663) (free of charge)
www.aaos.org

The academy provides education and practice management services for orthopaedic surgeons and allied health professionals. It also serves as an advocate for improved patient care and informs the public about the science of orthopaedics. The orthopaedist's scope of practice includes disorders of the body's bones, joints, ligaments, muscles, and tendons. For a single copy of an AAOS brochure, send a self-addressed stamped envelope to the address above or visit the AAOS Web site.

- **American College of Rheumatology/Association of Rheumatology Health Professionals**
1800 Century Place, Suite 250
Atlanta, GA 30345-4300
Phone: 404-633-3777
Fax: 404-633-1870
www.rheumatology.org

This association provides referrals to rheumatologists and physical and occupational therapists who have experience working with people who have rheumatic diseases. The organization also provides educational materials and guidelines about many different rheumatic diseases.

- **Arthritis Foundation**
1330 West Peachtree Street, Suite 100
Atlanta, GA 30309
Phone: 404-872-7100 or 800-568-4045 (free of charge)
or call your local chapter (listed in the telephone
directory)
www.arthritis.org

This is the main voluntary organization devoted to arthritis. The foundation publishes free pamphlets on many types of arthritis and a monthly magazine for members that provides up-to-date information on arthritis. The foundation can provide physician and clinic referrals. The American Juvenile Arthritis Organization (AJAO) is under the umbrella of the Arthritis Foundation. It shares the same address, phone numbers, and Web site.

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The mission of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a part of the Department of Health and Human Services' National Institutes of Health (NIH), is to support research into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases, the training of basic and clinical scientists to carry out this research, and the dissemination of information on research progress in these diseases. The National Institute of Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse is a public service sponsored by the NIAMS that provides health information and information sources. Additional information can be found on the NIAMS Web site at www.niams.nih.gov.



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